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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Horrobin, et al.		
Serial No.:	08/945,667	Group Art Unit:	1613
Filed:	January 28, 1998	Examiner:	Higel

FOR: 1,3-PROPANE DIOL DERIVATIVES AS BIOACTIVE AGENTS

ATTORNEY DOCKET NO.: 34237/170943

Assistant Commissioner for Patents
Washington, D.C. 20231

DATE: September 30, 2000

DECLARATION UNDER 37 C.F.R. § 1.132

I, Dr. Michael Winther, hereby declare as follows:

1. I am the Research Director of QuantaNova Canada Ltd., a subsidiary of Scotia Holdings PLC. I have a Ph.D. in Biochemistry from Stirling University, Scotland (1979) and a B.Sc. in Molecular Biology from the University of California at Santa Barbara (1975). I have worked in the pharmaceutical industry for over twenty years. I was at the Welcome Research Laboratories, located in Beckenham, London for 9 years, becoming Head of Microbial Development. I have been employed by Scotia Holdings since January 1989, initially as a Project Manager in the UK and later as President and Laboratory Director of the Canadian research facility, employing 80 staff. In my past twelve years I have been involved in numerous studies of fatty acids as therapeutic drugs. I have organized clinical trials of fatty acid based drugs and directed research in fatty acids. These studies have involved detailed examination of the genes involved in fatty acid metabolism and how they are regulated in health and disease. I have been an inventor in several patents and patent applications related to the use of fatty acids as drugs and for drugs that modify fatty acid metabolism.

2. I have reviewed and am familiar with the above-identified patent application. I am informed that the Examiner of the U.S. Patent and Trademark Office has rejected the claims of this application under 35 U.S.C. § 103(a) as being unpatentable over European Patent Publication No. 0,161,114. I understand more particularly that the examiner believes the invention to be obvious in light of the fact that a linolenic acid ester of 1,3-propanediol is disclosed.

3. As a worker of at least ordinary skill in the relevant art, I disagree with the Examiner's conclusion. Based on the disclosure of European publication and the problems sought to be solved by that disclosure, one skilled in the art of plant growth regulants clearly would understand that the linolenic acid disclosed in the patents is the n-3 series alpha-linolenic acid, and not the n-6 series gamma-linolenic acid recited in the claims.

4. More specifically, the term "linolenic acid" as used in the cited publication refers to the alpha-linolenic acid, which is commonly understood to be the delta-9,12,15 acid (i.e., alpha-linolenic acid), rather than the delta-6,9,12 acid (i.e., gamma-linolenic acid).

5. The gamma-linolenic acid compounds recited in the claims of the above-identified application are particularly closely related to the fatty acids in lipid barriers in the human body. Gamma-linolenic acid is beyond the delta-6-desaturase conversion of fatty acids in the body, while alpha-linolenic acid is not. Thus, a worker having ordinary skill in this art would not have been motivated to replace the alpha-linolenic acid esters disclosed in the '477 and '114 publications with gamma-linolenic acid esters with any reasonable expectation that the gamma linolenic acid esters would function as plant growth regulants.

6. The development of new products based on fatty acids has presented a number of difficulties. The naturally occurring sources of fatty acids contain a complex mixture of fatty acids, mainly as triglycerides. Such triglycerides are composed of a very complex mixture of fatty acid species linked to the glycerol backbone through ester linkages. These mixed-species triglycerides are not very suitable for pharmaceutical products as they have such a complex composition. Several groups have produced purified forms of fatty acids, such as EPA, which are converted to ethyl esters, since unconjugated or 'free' fatty acids are unpalatable. Our experience is that EPA-EPA diol has a far superior oral bioavailability compared to other forms of delivery of EPA. We believe that this enhanced efficiency of uptake and utilization of EPA when provided in the diol form is a critical factor in the success of EPA diol in cancer cachexia.

7. At least the benefits achieved by the used of the claimed compounds in treating cachexia would have been unexpected to one having ordinary skill in the art, and in particular, to one having ordinary skill in the art of plant growth regulants in view of the cited publication.

8. I declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001 and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dr. Michael Winther

Date: March 9, 2001

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